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10/511,050	10/12/2004	Masami Kusaka	Q101060	6207
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SUITE 800				
WASHINGTON, DC 20037				
EXAMINER				
HUYNH, CARLIC K				
ART UNIT		PAPER NUMBER		
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MAIL DATE		DELIVERY MODE		
03/11/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/511,050

Applicant(s)

KUSAKA ET AL.

Examiner

CARLIC K. HUYNH

Art Unit

1612

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 December 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) 1 and 8 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-893)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date 06 December 2007.

DETAILED ACTION

Receipt of applicants' amendments and remarks filed on December 19, 2007 is acknowledged.

Status of the Claims

1. Claims 1-8 are pending in the application, with claims 1 and 8 having been withdrawn, in the Response to Election/Restriction filed on August 17, 2007. Accordingly, claims 2-7 are being examined on the merits herein.

The objections to the Specification for the Abstract of the disclosure as containing legal phraseology of "said" have been withdrawn in view of Applicants' amendments.

The rejections made under 35 U.S.C. 112, first paragraph to "preventing hot flashes" have been withdrawn in view of Applicants' amendments.

Information Disclosure Statement

The Information Disclosure Statement submitted on December 6, 2007 is acknowledged.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

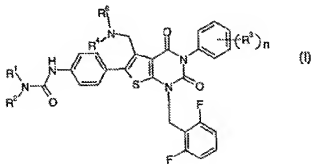
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

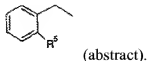
1. Determining the scope and contents of the prior art.
 2. Ascertaining the differences between the prior art and the claims at issue.
 3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
2. Claims 2-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furuya et al. (US 6,297,379) as evidenced by Hara et al. (*The Journal of Clinical Endocrinology & Metabolism*, 2003, Vol. 88, No. 4, pp. 1697-1704) and Freedman (*American Journal of Human Biology*, 2001, Vol. 13, pp. 453-464).

It is noted that Furuya et al. (US 6,297,379) is the National Stage of PCT publication WO00/56739 to Furuya et al. published on September 28, 2000.

Furuya et al. teach a method of treating sex hormone-dependent diseases comprising administering a compound of formula (I):



where R^6 is:



The compound of formula (I) has excellent gonadotropin releasing hormone (GnRH) antagonizing activity (abstract).

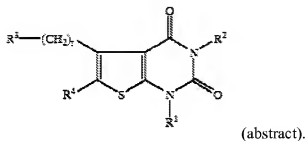
Regarding entering the brain as recited in instant claim 2, it is well known in the art that gonadotropin-releasing hormone (GnRH) is synthesized and released by the hypothalamus and is responsible for the release of follicle stimulating hormone (FSH) and lutenizing hormone (LH) from the anterior pituitary. It is also well known in the art that the anterior pituitary and hypothalamus are located at the brain stem. As evidenced by Hara et al., the gonadotropin-releasing hormone antagonist, TAK-013, was administered in female cynomolgus monkeys (page 1700). There was an LH surge in the plasma of monkeys treated with vehicle, however, there was no LH surge and LH plasma levels remained low in monkeys treated with TAK-013 (page 1700). Because gonadotropin-releasing hormone is synthesized in the hypothalamus, the gonadotropin-releasing hormone must reach and act in the brain in order to influence the release of lutenizing hormone. Thus it would be obvious that gonadotropin-releasing hormone enters the brain.

Regarding hot flash as recited in instant claim 7, Furuya et al. teach a method of treating sex hormone-dependent diseases (abstract). As evidenced by Freedman, hot flashes most commonly occur with the estrogen withdrawal at menopause (abstract). Freedman further discloses that gonadotropins are elevated at menopause and that there was a temporal association found between lutenizing hormone pluses and hot flash occurrence (page 459). Thus it would be considered obvious that hot flashes are a sex hormone-dependent condition.

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3. Claims 2-5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furuya et al. (US 6,048,863) as evidenced by Hara et al. (The Journal of Clinical Endocrinology & Metabolism, 2003, Vol. 88, No. 4, pp. 1697-1704) as applied to claim 2 above, and as further evidenced by Freedman (American Journal of Human Biology, 2001, Vol. 13, pp. 453-464).

Furuya et al. teach a method for treating disorders related to gonadotropin releasing hormone (GnRH) comprising administering a thienopyrimidine derivative of the formula:



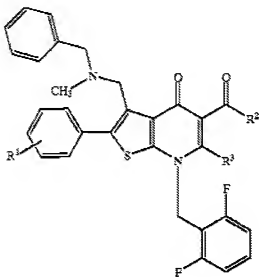
The thienopyrimidine derivative antagonizes gonadotropin-releasing hormone (column 2, lines 56-57).

Regarding hot flash as recited in instant claim 7, Furuya et al. teach a method of treating disorders related to gonadotropin releasing hormone (abstract). As evidenced by Freedman, hot flashes most commonly occur with the estrogen withdrawal at menopause (abstract). Freedman further discloses that gonadotropins are elevated at menopause and that there was a temporal association found between lutenizing hormone pluses and hot flash occurrence (page 459). Thus it would be considered obvious that hot flashes are a disorder related to gonadotropin releasing hormone.

4. Claims 2-4 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furuya et al. (US 6,001,850) as evidenced by Hara et al. (The Journal of Clinical Endocrinology &

Metabolism, 2003, Vol. 88, No. 4, pp. 1697-1704) and Freedman (American Journal of Human Biology, 2001, Vol. 13, pp. 453-464) as applied to claims 2 and 7 above.

Furuya et al. teach a method for treating sex hormone dependent diseases comprising administering a thienopyridine derivative having gonadotropin-releasing hormone antagonistic activity of the formula:

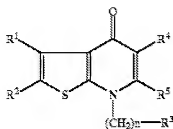


(abstract and column 36, lines 5-20).

The thienopyridine derivative has gonadotropin-releasing hormone antagonistic activity (abstract).

5. Claims 2-4 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furuya et al. (US 6,187,788) as evidenced by Hara et al. (The Journal of Clinical Endocrinology & Metabolism, 2003, Vol. 88, No. 4, pp. 1697-1704) and Freedman (American Journal of Human Biology, 2001, Vol. 13, pp. 453-464) as applied to claims 2 and 7 above.

Furuya et al. teach a method of treating a hormone dependent disease comprising administering a gonadotropin-releasing hormone antagonistic composition comprising a compound of the formula:



(abstract and column 116, lines 30-38).

Response to Arguments

6. Applicants' arguments, see "Remarks" filed on December 19, with respect to "Rejections under 35 U.S.C. § 103" to claims 2-5 and 7 or 2-7 has been fully considered and are not persuasive.

Applicants argue that each Furuya et al. reference (US 6,297,379; US 6,048,863; US 6,001,850; and US 6,187,788) teach the compounds are useful for treating sex hormone dependent cancers, prostatic hypertrophy, hysteromyoma, endometriosis, precocious puberty, amenorrhea, premenstrual syndrome, multiocular ovary syndrome and acne but not hot flashes. Applicants further argue that hot flashes occur under conditions where sex hormone levels are lowered.

Applicants also argue that Hara et al. (The Journal of Clinical Endocrinology & Metabolism, 2003, Vol. 88, No. 4, pp. 1697-1704) do not teach hot flashes but rather teach hormone-dependent diseases such as endometriosis, uterine leiomyomas and breast cancer.

Applicants also argue that Freedman (American Journal of Human Biology, 2001, Vol. 13, pp. 453-464) does not teach hot flashes are a sex hormone-derived condition because sex hormone levels are lowered in patients suffering from hot flashes. Applicants' submission of

Freedman (The American Journal of Medicine, 2005, Vol. 118, No. 12B, pages 124S-130S) is acknowledged.

These arguments are not persuasive.

Examiner points out that even though sex hormone levels are lowered in patients suffering from hot flashes, the sex hormone is still involved in the condition of hot flashes. Freedman (American Journal of Human Biology, 2001, Vol. 13, pp. 453-464) teach hot flashes most commonly occur with the estrogen withdrawal at menopause (abstract), suggesting that the lowering of estrogen is involved with hot flash. Estrogen is still involved in the hot flash condition and thus hot flash is considered a sex hormone-dependent condition.

Double Patenting

Obviousness-Type

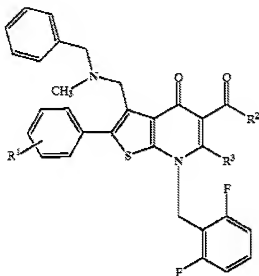
The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 4 and 7 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 13 of Furuya et al. (US 6,001,850) as evidenced by Freedman (American Journal of Human Biology, 2001, Vol. 13, pp. 453-464).

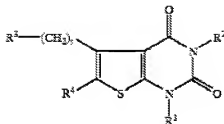
Claim 13 of Furuya et al. is directed to a method of treating a gonadotropin-releasing hormone derived disorder comprising administering a compound of formula:



Freedman discloses that hot flashes most commonly occur with the estrogen withdrawal at menopause (abstract). Freedman further discloses that gonadotropins are elevated at menopause and that there was a temporal association found between lutenizing hormone pluses and hot flash occurrence (page 459). Thus it would be considered obvious that hot flashes are a gonadotropin-releasing hormone derived disorder.

8. Claims 4 and 7 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 8 of Furuya et al. (US 6,048,863) as evidenced by Freedman (American Journal of Human Biology, 2001, Vol. 13, pp. 453-464).

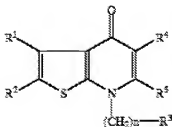
Claim 8 of Furuya et al. is directed to a method of treating a sex hormone dependent disease comprising administering a compound of formula:



Freedman discloses that hot flashes most commonly occur with the estrogen withdrawal at menopause (abstract). Freedman further discloses that gonadotropins are elevated at menopause and that there was a temporal association found between lutenizing hormone pluses and hot flash occurrence (page 459). Thus it would be considered obvious that hot flashes are a sex hormone dependent disease.

9. Claims 4 and 7 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 4 of Furuya et al. (US 6,187,788) as evidenced by Freedman (American Journal of Human Biology, 2001, Vol. 13, pp. 453-464).

Claim 4 of Furuya et al. is directed at a method of treating a gonadotropin-releasing hormone dependent disorder comprising administering a compound of formula:



Freedman discloses that hot flashes most commonly occur with the estrogen withdrawal at menopause (abstract). Freedman further discloses that gonadotropins are elevated at

menopause and that there was a temporal association found between lutenizing hormone pluses and hot flash occurrence (page 459). Thus it would be considered obvious that hot flashes are a gonadotropin-releasing hormone derived disorder.

Response to Arguments

10. Applicants' arguments, see "Remarks" filed on December 19, 2007, with respect to "Obviousness-type Double patenting Rejections" to claims 4 and 7 has been fully considered and are not persuasive. It is noted Applicants use the same arguments as above in "Rejections under 35 U.S.C. § 103". Examiner argues as above in response to the arguments directed at "Rejections under 35 U.S.C. § 103".

Conclusion

11. No claims are allowable.
12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carlic K. Huynh whose telephone number is 571-272-5574. The examiner can normally be reached on Monday to Friday, 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gollamudi S Kishore, Ph.D/
Primary Examiner, Art Unit 1612

ckh